

IN THE CLAIMS:

1. (Currently amended) A method for controlling or up-regulating the availability or activity of a protein reducing binding of a ubiquitin-proteasome system to a cell surface receptor, the method comprising:

contacting a cell with a peptide that specifically inhibits the interaction of an ubiquitin-proteasome segment with an ubiquitin-proteasome binding site comprising xEFIxxDx (SEQ ID NO: 1), wherein D is aspartic acid, E is glutamic acid, F is phenylalanine, I is isoleucine and x is any other amino acid, wherein said peptide corresponds to the motif of SEQ ID NO: 1;

regulating binding of a thus reducing the incidence of the ubiquitin-proteasome system at a ubiquitin-proteasome binding site of said protein to the cell surface receptor.

2. (Canceled).

3. (Withdrawn) A method for controlling the signal transduction capability of a cell surface receptor comprising providing an inhibitor capable of inhibiting proteolytic cleavage of said receptor.

4. (Withdrawn) The method according to claim 3 wherein said inhibitor is capable of inhibiting proteolytic cleavage of an intra-cellular part of said receptor.

5. (Withdrawn) The method according to claim 3, wherein said inhibitor is capable of inhibiting proteolytic cleavage of an intra-cellular part of said receptor.

6. (Withdrawn) The method according to claim 3, wherein said receptor is a hormone receptor.

7. (Withdrawn) The method according to claim 6, wherein said receptor is a growth hormone receptor.

8. (Currently amended) The method according to claim 1, wherein said protein cell surface receptor is a transport protein.

9. (Previously presented) The method according to claim 8, wherein said transport protein is Glut4 insulin regulated glucose transporter.

10-11. (Canceled).

12. (Withdrawn) The method according to claim 3, wherein said inhibitor is capable of inhibiting proteolytic cleavage of a cell surface receptor.

13. (Withdrawn) The method according to claim 12, wherein said inhibitor is capable of inhibiting proteolytic cleavage of an intra-cellular part of said receptor.

14. (Withdrawn) The method according to claim 13, wherein said inhibitor is selected from the group of proteasome inhibitors consisting of MG132, carboxybenzyl-leucyl-leucyl-leucinal, lactacystin, carboxybenzyl-leucyl-leucyl vinylsulfone and the β -lacton form of lactacystin.

15. (Withdrawn) The method according to claim 13, wherein said inhibitor comprises a polypeptide that is derived from, competes with, or binds to an amino acid sequence located at or around a ubiquitin-proteasome system binding site located in an intra-cellular part of a cell-surface receptor.

16. (Withdrawn) The method according to claim 15 wherein, said ubiquitin-proteasome system binding site comprises the amino acid sequence motif xEFlxxDx or a sequence essentially corresponding thereto, wherein D is aspartic acid, E is glutamic acid, F is phenylalanine, I is isoleucine and X is any other amino acid.

17. (Withdrawn) The method according to claim 16, wherein said ubiquitin-proteasome system binding site comprises an amino acid sequence selected from the group consisting of DDSWVEFIELDI (SEQ ID NO:2) and DSWVEFIELD (SEQ ID NO:3).

18. (Withdrawn) The method according to claim 12, wherein said inhibitor is capable of inhibiting proteolytic cleavage of extra-cellular part of said receptor.

19. (Withdrawn) The method according to claim 18, wherein said extra-cellular part comprises an approximately 60 kDa fragment of an extra-cellular domain of the growth hormone receptor.

20. (Withdrawn) The method according to claim 18, wherein said inhibitor comprises a polypeptide that is derived from, competes with or binds to an amino acid sequence located at or around a proteolytic cleavage signal site located in an extra-cellular part of said receptor.

21. (Withdrawn) The method according to claim 20, wherein said cleavage signal site comprises the amino acid sequence CEEDFYR (SEQ ID NO:7).

22. (Currently amended) The inhibitor method according to claim 10 1, wherein said polypeptide interferes with said ubiquitin proteasome system by binding to a ubiquitin-proteasome system binding site is located in the intra-cellular part of [[a]] said cell-surface receptor.

23. (Canceled)

24. (Withdrawn) The inhibitor according to claim 10, wherein said polypeptide interferes with said ubiquitin-proteasome system by binding to an amino acid sequence located at or around a proteolytic cleavage signal site located in an extra-cellular part of a receptor.

25. (Withdrawn) The inhibitor peptide according to claim 24, wherein said cleavage signal site comprises an amino acid sequence CEEDFYR (SEQ ID NO:7).

26. (Canceled).

27. (Currently amended) ~~A pharmaceutical composition~~ The method according to claim 26 ~~for regulating 1, wherein said peptide is capable of regulating~~ the activity of a hormone.

28. (Canceled)

29. (Currently amended) ~~The pharmaceutical composition~~ method according to claim 26 1, wherein said inhibitor is used for peptide is capable of controlling the availability and or signal transduction capability of [[a]] said cell surface receptor.

30-32. (Canceled)

33. (Currently amended) The method according to claim 1, wherein, ~~said regulating binding of the a ubiquitin-proteasome system at a ubiquitin-proteasome binding site of said protein comprises controlling or up-regulating hormone activity by using an inhibitor polypeptide which said peptide interferes with said ubiquitin-proteasome system regulation of the cell surface receptors of [[a]] said cell.~~

34. (Withdrawn) The method according to claim 6, wherein said hormone receptor is selected from the group consisting of amino acid derivatives, prostaglandins, peptides or protein hormone receptors.

35. (Currently amended) The inhibitor method according to claim 10 1, wherein said polypeptide peptide interferes with said ubiquitin-proteasome system regulation of the cell surface receptors receptor of [[a]] the cell by inhibiting ligand-induced receptor uptake.

36. (Currently amended) The inhibitor method according to claim 10 1, wherein said polypeptide peptide interferes with said ubiquitin-proteasome system regulation of the cell surface receptors receptor of [[a]] the cell by inhibiting receptor degradation caused by endocytosis.